REMARKS

Independent claim 5 is amended for purposes of clarity. Support for this amendment can be found, for example, on page 17 of the published application. No new matter has been added.

REJECTIONS UNDER 35 U.S.C. § 102(b)

RATGE

The Office Action rejects claims 5-8, 10-12 as anticipated under 35 U.S.C. § 102(b) by Ratge *et al.* (J Clin Virol. 2002, Vol 24, pp. 161-172; hereinafter "Ratge"). In particular, the Office Action points to pages 163-165 and figure 1 to allege that Ratge anticipates the present invention because the reference teaches a method for nucleic acid detection comprising the steps of nucleic acid isolation of infectious agent, nucleic acid amplification of the pathogen and performing real time PCR on the pathogenic nucleic acid of the infectious agent.

A patent claim is anticipated by prior art if a single prior art reference discloses every limitation of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of Cal., 814 F.2d 628, 631 (Fed. Cir.1987). If a single claim limitation is missing from the reference, then the reference does not anticipate the claim. Atlas Powder Co. v. E.I. du Pont *de Nemours* & Co., 750 F.2d 1569, 224 USPQ 409 (Fed.Cir.1984).

In response, without acceding to the merit of the rejection and solely to expedite allowance of the pending claims, Applicants have herein amended independent claim 5. As amended, claim 5 is directed to a method for detecting a nucleic acid of a pathogenic infectious agent comprising the sequential steps of: (a) isolating the nucleic acid of the pathogenic infectious agent, (b) pre-amplifying the nucleic acid of the pathogenic infectious agent, and (c) performing Real Time PCR on the nucleic acid of the pathogenic agent that is pre-amplified in step (b).

Ratge discloses the use of RT-PCR (*i.e.* reverse transcription), rather than real-time PCR. As such, Applicants respectfully contend that the comments on page 3 of the Office Action:

"Ratge et al. teach a method... for nucleic acid (RNA) detection comprising the steps of ....and performing ...real time PCR" are not correct. Rather, Ratge discloses using the following steps to detect HCV: (1) reverse transcription (RT) of the target virus RNA into cDNA, with no subsequent PCR step involved; and (2) nested PCR or in equivalence two-round PCR on the reversly transcribed cDNA for amplification and detection (*see* pages 163 and 164 of Ratge). Therefore, the method has been termed "two-round rapid-cycle RT-PCR", in which "RT" stands for reverse transcription. Applicants respectfully highlight that the term "RT-PCR" being used throughout Ratge stands for "reverse transcription PCR," and that real-time PCR was not mentioned or used in the detection process of Ratge.

To be anticipating, a prior art reference must disclose each and every limitation of the claimed invention, must be enabling, and must describe the claimed invention sufficiently to have placed it in possession of a person of ordinary skill in the field of the invention. In re Paulsen, 30 F.3d 1475, 1478-79, 31 USPQ2d 1671, 1673 (Fed.Cir.1994). This means that a person of ordinary skill in the field could combine the description of the invention in the anticipatory reference with that person's own knowledge to make the claimed invention. Elan Pharms., Inc. v. Mayo Found. for Med. Educ. & Research, 346 F.3d 1051, 1055 (Fed.Cir.2003). Furthermore, "... [the] absence from the reference of any claimed element negates anticipation." Kloster Speedsteel AB v. Crucible Inc., 793 F.2d 1565, 230 U.S.P.Q.2d 1051 (Fed.Cir. 1987).

Thus, since Ratge fails to expressly or inherently teach the present invention as claimed in amended claim 5, Ratge fails to anticipate the present invention. With respect to rejected claims 6-8 and 10-12 , which depend on claim 5, it is respectfully pointed out that typically if an accused infringer does not infringe an independent claim, it cannot infringe any claim that depends from the independent claim. Wahpeton Canvas Co. v. Frontier, Inc., 870 F.2d 1546 (Fed. Cir. 1989). Thus, in view of the amendment made to claim 5 and the above, Applicants respectfully request that rejection of claims 5-8, and 10-12 under 35 U.S.C. § 102(b) as being anticipated by Ratge be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 102(e)

PEIRIS I

The Office Action rejects claims 5-6, and 8-16 as being anticipated under 35 U.S.C. § 102(e) by U.S. patent No. 7,375,202 to Peiris *et al.* (hereinafter "Peiris I"). In particular, the Office Action alleges that Applicants' prior response was unpersuasive because the claims do not recite pre-amplification, nor require the PCR product from the first round PCR for performing real-time PCR. The Office Action states that this is so because the claims recite "amplifying the nucleic acid of the infectious agent and performing real time PCR on the nucleic acid of the pathogenic agent, which indicates two separate PCR reactions that do not require the use of amplified nucleic acid from the first round PCR to perform real-time PCR. The Office Action further alleges that Peiris I *does* teach two separate PCR reactions (RT-PCR and real time PCR) using the nucleic acid of the pathogenic agent, and the scope of the invention as claimed does not exclude amplification by RT-PCR and a second real-time PCR using the nucleic acid of the pathogenic agent.

In response, Applicants respectfully disagree with the propriety of this anticipation rejection. First, Applicants point out that a patent claim is anticipated by prior art if a single prior art reference discloses every limitation of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of Cal., 814 F.2d 628, 631 (Fed. Cir.1987). If a single claim limitation is missing from the reference, then the reference does not anticipate the claim. Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569 (Fed.Cir.1984).

Without acceding to the merit of the rejection and solely to expedite allowance of the pending claims, Applicants have herein amended independent claim 5. As amended, claim 5 is directed to a method for detecting a nucleic acid of a pathogenic infectious agent comprising the sequential steps of: (a) isolating the nucleic acid of the pathogenic infectious agent, (b) pre-amplifying the nucleic acid of the pathogenic infectious agent, and (c) performing Real Time

PCR on the nucleic acid of the pathogenic agent that is pre-amplified in step (b). Applicants respectfully submit that Peiris I does not disclose a method that recites the sequential steps, as recited in amended claim 5. Applicants respectfully highlight that if a single claim limitation is missing from the reference, then the reference does not anticipate the claim.

The portions of Peiris I pointed out by the Office Action (namely, columns 33-34, section 6.7) disclose multiple independent experiments or procedures. Specifically, column 33 discloses a distinct and independent procedure consisting of a step of RT-PCR performed directly on the clinical specimen (*see* lines 16-51 and specifically lines 34-36), or a different procedure, beginning with culturing of the virus from two patients followed by a RT-PCR step (*see* lines 54-58). There is no teaching in Peiris I of the step of RT-PCR being preceded by a pre-amplification step, as recited in pending claim 5.

Further in contrary to the assertion of the Office Action, column 34 discloses yet another distinct and independent procedure, which includes RNA extraction, reverse transcription, followed by PCR (*see* lines 1-46). Here, there is no teaching of RT-PCR, nor any pre-amplification step before RT-PCR. Column 34 of Peiris I also discloses another procedure, which includes an extraction step (*see* line 50) followed by a reverse transcription step (*see* line 52). There is a DNA amplification step (*see* line 56) followed by a PCR step (*see* line 62). However, in contrast to the present invention, there is no teaching of a pre-amplification step before the RT-PCR step. In other words, the amplification of Peiris is the polynucleotide-amplifying nature of Peiris's real-time PCR step and not a further independent pre-amplification step prior to real-time PCR step, as taught and claimed in the present invention.

It is acknowledged that amplification by itself is not new and RT-PCR by itself also is not new. However, the claimed invention is not directed to these isolated steps. None of the approaches of Peiris I teach or suggest the method recited in claim 5, which provides, after isolation of a nucleic acid, a pre-amplifying step which is then followed by a Real Time PCR step. Applicants respectfully highlight that the present invention provides that the use of a pre-amplification step prior to RT-PCR provides a surprising range of benefits including greater detection levels, improved sensitivity and quicker times than provided by conventional PCR techniques alone (*see* for example paragraph [0076] of the published application). It would be

improper to pick different steps from distinct procedures in Peiris I and assert that they are used together and therefore anticipate pending claims 5-6 and 8-16.

Peiris I discloses two preferred embodiments (*see* col. 27, lines 25 to 54). In one embodiment, the presence of hSARS virus is detected in the sample by RTPCR. In a more preferred embodiment, the invention provides a real-time quantitative PCR assay to detect the presence of hSARS virus in a biological sample by subjecting the cDNA obtained by reverse transcription of the extracted total RNA from the sample to PCR reactions using specific primers. The fluorescence signals from these reactions are captured at the end of extension steps as the PCR product is generated over a range of the thermal cycles, thereby allowing the quantitative determination of the viral load in the sample based on an amplification pot. The two embodiments of Peiris I describe two methods of detection, one using RT-PCR (reverse transcription PCR) and the other using real-time PCR. Peiris I does not suggest the use of real-time PCR on the sample already detected by RT-PCR.

The RT-PCR (reverse transcription PCR) described in Peiris I at col. 27, lines 26-41 and col. 33, line 54 to col. 34, line 47 is a discrete detection method from the real-time PCR described in Peiris I at col. 27, lines 41-54 and col. 34, lines 48 to col. 35, line 3. Furthermore, col. 27, lines 42-45 only describe the use of "a real-time quantitative PCR assay to detect...by subjecting the cDNA obtained by reverse transcription of the extracted total RNA from the sample..." Reverse transcription process itself does not involve amplification. Therefore, lines 26-41 of Peiris I describes two separate detection methods: A) by reverse transcription PCR; or B) by real-time PCR of the cDNA obtained by reverse transcription of total RNA from sample. There is no amplification (*i.e.* pre-amplification) performed before the amplification that takes place in the PCR process in Method A and the real-time PCR in Method B.

To be anticipating, a prior art reference must disclose each and every limitation of the claimed invention, must be enabling, and must describe the claimed invention sufficiently to have placed it in possession of a person of ordinary skill in the field of the invention. In re Paulsen, 30 F.3d 1475, 1478-79, 31 USPQ2d 1671, 1673 (Fed.Cir.1994). This means that a person of ordinary skill in the field could combine the description of the invention in the anticipatory reference with that person's own knowledge to make the claimed invention. Elan

Pharms., Inc. v. Mayo Found. for Med. Educ. & Research, 346 F.3d 1051, 1055 (Fed.Cir.2003). Furthermore, "... [the] absence from the reference of any claimed element negates anticipation." Kloster Speedsteel AB v. Crucible Inc., 793 F.2d 1565, 230 U.S.P.Q.2d 1051 (Fed.Cir. 1987).

Thus, since Peiris I fails to expressly or inherently teach the present invention as claimed in amended claim 5, Peiris I fails to anticipate the present invention. With respect to rejected claims 6-8 and 8-16, which depend on claim 5, it is respectfully pointed out that typically if an accused infringer does not infringe an independent claim, it cannot infringe any claim that depends from the independent claim. Wahpeton Canvas Co. v. Frontier, Inc., 870 F.2d 1546 (Fed. Cir. 1989). Thus, in view of the above, withdrawal of the rejection of claims 5-6 and 8-16 under 35 U.S.C. §102(e) as being anticipated by Peiris I is respectfully requested.

PEIRIS II

Claims 5-16 have also been rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. patent No. 7,267,942 to Peiris *et al.* (hereinafter "Peiris II"). In particular, the Office Action alleges that Applicants' prior response was unpersuasive because the claims do not recite pre-amplification, nor require the PCR product from the first round PCR for performing real-time PCR. The Office Action states that this is so because the claims recite "amplifying the nucleic acid of the infectious agent and performing real time PCR on the nucleic acid of the pathogenic agent, which indicates two separate PCR reactions that do not require the use of amplified nucleic acid from the first round PCR to perform real-time PCR. The Office Action further alleges that Peiris I *does* teach two separate PCR reactions (RT-PCR and real time PCR) using the nucleic acid of the pathogenic agent, and the scope of the invention as claimed does not exclude amplification by RT-PCR and a second real-time PCR using the nucleic acid of the pathogenic agent.

In response, for at least the same reasons as outlined *supra* for refuting Peiris I as an anticipatory reference, Applicants incorporate herein and repeat said position regarding Peiris II. Applicants respectfully point out that a patent claim is anticipated by prior art if a single prior art reference discloses every limitation of the claim. "A claim is anticipated only if each and every

element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of Cal., 814 F.2d 628, 631 (Fed. Cir.1987). If a single claim limitation is missing from the reference, then the reference does not anticipate the claim. Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569 (Fed.Cir.1984).

Without acceding to the merit of the rejection and solely to expedite allowance of the pending claims, Applicants have herein amended independent claim 5. As amended, claim 5 is directed to a method for detecting a nucleic acid of a pathogenic infectious agent comprising the sequential steps of: (a) isolating the nucleic acid of the pathogenic infectious agent, (b) pre-amplifying the nucleic acid of the pathogenic infectious agent, and (c) performing Real Time PCR on the nucleic acid of the pathogenic agent that is pre-amplified in step (b). Applicants respectfully submit that Peiris I does not disclose a method that recites the sequential steps, as recited in amended claim 5. Applicants respectfully highlight that if a single claim limitation is missing from the reference, then the reference does not anticipate the claim.

Applicants respectfully submit that Peiris II does not teach a method for detection of nucleic acid of a pathogenic infectious agent that comprises the sequential steps of amplifying the nucleic acid of a pathogenic infectious agent followed by performing Real-Time PCR on the nucleic acid of the pathogenic infectious agent. The section in Peiris II that was previously cited (column 11, lines 16-47) discloses the use of real-time quantitative PCR to detect the presence of hSARS virus. The amplification disclosed therein refers to the amplification that is part of the real-time PCR. Claim 5 refers to a pre-amplification step (*see* amended claim 5), separate from the real-time PCR step. As noted *supra*, neither Peiris I or Peiris II teach or suggest such a separate pre-amplification step, and that the use of a pre-amplification step prior to performing real-time PCR provides a surprising range of benefits. In particular, as stated in paragraph [0076] of the published application:

> After the target SARS coronavirus viral RNA molecules (10) are extracted from the biological sample the amount of RNA molecules in the sample may not be sufficient to be detected. Therefore, a portion of the SARS coronavirus viral RNA

> molecule is replicated to a target nucleic acid molecule by an appropriate amplification technique, for example, polymerase chain reaction (PCR) or NASBA or RT-PCR. The target nucleic acid molecules may then be detected by suitable methods. The use of a pre-amplification step prior to RT-PCR surprisingly provides a range of benefits including greater detection levels, improved sensitivity and quicker times than provided by conventional PCR techniques alone. (emphasis added).

Peiris II dislcoses a method which involves real-time PCR (*see* col. 11, lines 16-47). In Peiris II, the cDNA obtained by reverse transcription ("RT") is subject to real-time PCR reaction. Applicants respectfully highlight that RT is a process in which RNA is reverse transcribed to cDNA using reverse transcriptase. There is no amplification before real-time PCR. Peiris II mentions "detecting the amplified product using a probe" (*see* col. 11, line 29). Real time PCR is used to amplify and simultaneously quantify a targeted DNA molecule and the amplified product is the product of the amplification during the real-time PCR. That is, in contrast to the presently claimed invention, there is no amplification (*i.e.* pre-amplification) being performed before the amplification that takes place in the real-time PCR process. In other words, in contrast to the present invention, there is no teaching in Peiris II of a pre-amplification step before the RT-PCR step, as presently claimed. Moreover, in contrast to Peiris I and II, in the present invention, after the pre-amplification step (where the nucleic acid of the pathogenic infectious agent is pre-amplified), a separate step is performed on said nucleic acid, namely real-time PCR.

To be anticipating, a prior art reference must disclose each and every limitation of the claimed invention, must be enabling, and must describe the claimed invention sufficiently to have placed it in possession of a person of ordinary skill in the field of the invention. In re Paulsen, 30 F.3d 1475, 1478-79, 31 USPQ2d 1671, 1673 (Fed.Cir.1994). This means that a person of ordinary skill in the field could combine the description of the invention in the anticipatory reference with that person's own knowledge to make the claimed invention. Elan Pharms., Inc. v. Mayo Found. for Med. Educ. & Research, 346 F.3d 1051, 1055 (Fed.Cir.2003). Furthermore, "... [the] absence from the reference of any claimed element negates anticipation." Kloster Speedsteel AB v. Crucible Inc., 793 F.2d 1565, 230 U.S.P.Q.2d 1051 (Fed.Cir. 1987).

Thus, since Peiris II fails to expressly or inherently teach the present invention as claimed in amended claim 5, Peiris II fails to anticipate the present invention. With respect to rejected claims 6-16, which depend on claim 5, it is respectfully pointed out that typically if an accused infringer does not infringe an independent claim, it cannot infringe any claim that depends from the independent claim. Wahpeton Canvas Co. v. Frontier, Inc., 870 F.2d 1546 (Fed. Cir. 1989). Thus, in view of the above, withdrawal of the rejection of claims 5-16 under 35 U.S.C. §102(e) as being anticipated by Peiris II is respectfully requested.

There being no other outstanding issues, it is believed that the application is in condition for allowance, and such action is respectfully requested. Should the Examiner believe that anything further is desirable in order to place the application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

The undersigned hereby authorizes the Commissioner to charge any fee insufficiency and credit any overpayment associated with this submission to Deposit Account No. 08-1935.

Respectfully submitted,

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